UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**

PLAINTIFFS' BRIEF IN SUPPORT OF *DAUBERT* MOTION TO PRECLUDE OPINIONS OF DEFENSE EXPERT MICHAEL BOTTORFF, Pharm. D.

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PRELIMINARY STATEMENT

This Court has held: "The Valsartan MDL arose from an extensive Food and Drug Administration ["FDA"] recall in the U.S. of generic hypertensive, prescription drugs ["Valsartan" or "Valsartan-containing drugs" or "VCD'S"]. To be clear, as used herein, the term "VCD" refers to valsartan-containing drugs that were contaminated with probable genotoxic human carcinogens in the form of nitrosamines, N-nitrosodimethylamine ("NDMA") and N- N-nitrosodiethylamine ("NDEA")." *In re Valsartan, Losartan & Irbesartan Prods. Liab. Litig*., 2023 WL 1818922, 2023 US Dist. LEXIS 21112 (D.N.J. 2023) at *115-116.

As recognized by this Court: "It is further incontrovertible in the morass of factual and legal arguments here that the contamination resulted from defendants' non-compliance of cGMPs at some level." *In re Valsartan, Losartan & Irbesartan Prods. Liab. Litig*., 2023 WL 1818922, 2023 US Dist. LEXIS 21112 (D.N.J. 2023) at *149.

Defense Expert Michael Bottorff, Pharm. D. is a pharmacist and professor at the College of Pharmacy at Manchester University in Ft. Wayne, Indiana. His expert reports discuss the pharmacokinetics of valsartan and N-nitrosodimethylamine (NDMA) and N-nitrosodimethylamine (NDEA) and specific to this motion, Dr. Bottorff offers opinions that valsartan drug products contaminated with NDMA/NDEA had the same bioequivalence as valsartan drugs that were not contaminated with NDMA/NDEA even though he is unable to point to any scientific study for support. Dr. Bottorff further offers an opinion only at his deposition that contaminated valsartan drug products would have the same monetary value as non-contaminated valsartan drug products. While Dr. Bottorff then states he is not offering any testimony as an expert on monetary value of valsartan, this motion seeks preclusion of any attempted proffering of this opinion, which is only stated in deposition testimony and not in his expert reports.

THE *DAUBERT* STANDARD

The *Daubert* Standard and Rule 702 Requirements

The Federal Rules of Evidence 702 governs the admissibility of expert testimony in federal court. The law in this area is well established for the issues on this motion. A party offering a proposed expert has the burden to establish the admissibility of the expert's testimony is based upon reliable methodology and reliable application of that methodology. *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig*. 858 F. 3d 187 at 800 (3d Cir., 2017). Rule 702 requires that an expert have "specialized knowledge" that will assist the fact finder to understand the evidence or determine a fact in issue; that the witness be qualified by knowledge, skill, experience, training or education. An expert witness may testify only if the testimony is based upon sufficient facts or data; the testimony is the product of reliable principles and methods, and the witness has applied these principles and methods reliably to the facts in issue.

The Third Circuit in *In re Paoli R.R. Yard PCB Litigation*, 35 F. 3d 717, 742 (3d Cir, 1994) stated the well-known standard that an "expert's opinions must be based on the methods and procedures of science, rather than on subjective belief or unsupported speculation." An expert must have "good grounds" for the opinion being offered which includes each step of the expert's analysis. *Paoli* also reviews the Third Circuit reliability factors to be considered which include how and when an expert's methodology is used outside of litigation. *Id*., at 742. Any step of the analysis which renders the expert's analysis to be unreliable renders the expert's testimony inadmissible. "*Daubert*'s gatekeeping requirement .... make[s] certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" *Elcock v. Kmart Corp.*, 233 F.3d 734, 746 (3d Cir. 2000) (quoting *Kumho Tire Co. v. Carmichael*,

526 U.S. 137, 152 (1999)); *see also Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F.Supp.2d 584, 594 (D.N.J.2002*), aff'd,* 68 Fed. Appx. 356 (3d Cir. 2003).

The Third Circuit considers the following factors when determining an expert's reliability: (i) whether the expert's proposed testimony grows naturally and directly out of research the expert has conducted independent of the litigation; (ii) whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion; (iii) whether the expert has adequately accounted for alternative explanations. *Magistrini*, 180 F. Supp. 2d at 594–95, internal citations omitted. Using these standards, this Circuit has excluded expert testimony that "failed to consistently apply the scientific methods … articulate[d], … deviated from or downplayed certain well-established principles of [the] field, and … inconsistently applied methods and standards to the data so as to support [an] a priori opinion." *Zoloft*, 858 F.3d at 792.

It is established that in order to meet the *Daubert* standard, an expert witness must not only have good grounds for their opinion, but it must be based on the "methods and procedures of science rather than on subjective belief or unsupported speculation". *In re Johnson & Johnson Talcum Powder Prods. Mktg. Sales Practices and Prods. Litig*., 509 F. Supp. 3d 116, at 131 (NJDC, 2020), citing *In re Paoli*, 35 F. 3d at 742.

Opinions that deal in "possibilities" are not sufficient to support admissibility of expert testimony. *Danley v. Bayer (In re Mirena IUD Prods. Liab. Litig*., 169 F. Supp. 3d 396 at 433 (SDNY, 2016).

FRCP 26(a)(2)

Federal Rule of Civil Procedure 26(a)(2) governs the disclosure of expert testimony and specifically the contents of an expert report. This Rule states the following: "The report must contain: (i) a complete statement of all opinions the witness will express and the basis and reasons

for them; (ii) the facts or data considered by the witness in forming them ….” Fed. R. Civ. P. 26(a)(2)(B)(i) & (ii). A failure to submit an expert report that complies with Rule 26 is an independent basis for the exclusion of the expert’s testimony. *See, e.g., Meyers v. Nat’l R.R. Pass. Corp. (Amtrak)*, 619 F.3d 729, 734 (7th Cir. 2010) (“The consequence of non-compliance with Rule 26(a)(2)(B) is exclusion of an expert’s testimony[.]” (internal quotations and citations omitted)).

ARGUMENT

A. Dr. Bottorff’s Opinion that Contaminated Valsartan Containing Drugs are Bioequivalent to VCDs that are Not Contaminated Has No Scientific Support

Dr. Bottorff produced two expert reports for this litigation that focus primarily on the pharmacokinetics of valsartan, a general causation report dated August 2, 2021,[1] and another report dated January 12, 2022.[2] Pharmacokinetics is the study of how drug substances interact with the human body for the drug’s entire duration of exposure. Both of Dr. Bottorff’s expert reports are remarkably lacking in supportive references and contain large swaths of statements and discussion that are not documented by any source material, including for the opinions which are the subject of this motion to preclude.

While Dr. Bottorff may have general pharmacy knowledge and experience from his training and background, this does not excuse a meaningful lack of confirmatory scientific references in which to verify the accuracy and substance of Dr. Bottorff’s explanations and findings in his reports. Without adequate scientific references citing to the statements and information he provides in his reports, we are left to simply “accept” wholesale sections of his

[1] Expert Report of Michael Bottorff dated 8-02-2021, attached as Ex. A.
[2] Expert Report of Michael Bottorff dated 1-12-2022, attached as Ex. B.

expert report discussion without the ability to verify via cited scientific references. This does not meet the *Daubert* reliability standard and unsupported subjective pronouncements by this expert are plainly unreliable as they cannot be tested via examination of cited scientific authority. Indeed, the first 20 pages of Dr. Bottorff's August 2, 2021 expert report only cites 8 footnote references for all the material that is covered. Similarly, the January 12, 2022 expert report only has 11 reference citations in the first 22 pages. Most of Dr. Bottorff's analysis in these sections have no authority cited. In Dr. Bottorff's expert report dated August 2, 2021, he states on p. 20,

> Valsartan has been in clinical use for more than three decades, and thousands of research studies ranging from in vitro pharmacology, animal pharmacology and toxicology, and human studies have been conducted on this drug.[3]

In this same report, on p. 23, Dr. Bottorff offers this unsupported conclusion:

> In any event, there is no known or identified interaction with these transporters and NDMA/NDEA or other nitrosamines, so there is no known interaction of NDMA/NDEA with the hepatic uptake or biliary excretion of valsartan, and thus no know(n) alteration in valsartan's clinical effects.[4]

However, despite "thousands of research studies" with "no known or identified interaction" by NDMA/NDEA, it is glaring that Dr. Bottorff cannot point to a single bioequivalence study to support his opinion that NDMA/NDEA contaminated valsartan drug products do not affect its efficacy and chemical action within the human body. Dr. Bottorff cannot point to any study that shows valsartan containing drugs contaminated with NDMA/NDEA do not reduce the effectiveness of the valsartan drug by 1% or 10% or any another percentage. Dr. Bottorff's opinion as set forth in his January 12, 2022 expert report is based on his interpretation of bioequivalence studies conducted prior to valsartan being contaminated with nitrosamines.[5]

[3] Bottorff Report 8-02-2021, p. 20, attached as Ex. A.
[4] Bottorff Report 8-02-2021, p. 23, attached as Ex. A.
[5] Bottorff Report 1-12-2022, p. 30-32, attached as Ex. B.

There is zero evidence these bioequivalence studies were conducted using NDMA/NDEA contaminated valsartan containing drugs. Without proof the bioequivalence studies used contaminated valsartan for the testing, Dr. Bottorff cannot draw a scientifically supported conclusion that these same studies establish NDMA/NDEA contaminated VCDs work in the exact same manner as non-contaminated VCDs. We have only his speculation and *ipse dixit* for this opinion. Dr. Bottorff was questioned numerous times at his deposition on March 25, 2022 about not knowing that the valsartan bioequivalence studies he relied on did not evaluate valsartan containing nitrosamines. Dr. Bottorff was first questioned on Teva's bioequivalency studies and testified as follows:

[redacted]

Dr. Bottorff testified similarly in regard to Prinston's bioequivalency testing:

[redacted]

[6] Bottorff Dep. 3-25-2022, p. 46:6-48:13 (emphasis added), attached as Ex. C.

[redacted]

Dr. Bottorff also testified that he didn't know if the valsartan testing by Hetero for their bioequivalence studies were actually contaminated with nitrosamines:

[redacted]

In regard to Mylan bioequivalence studies, Dr. Bottorff again conceded that he didn't know if the valsartan tested was contaminated:

[redacted]

[7] Bottorff Dep. 3-25-2022, p. 55:20-56:4; 81:6-82:3 (emphasis added), attached as Ex. C.
[8] Bottorff Dep. 3-25-2022, p. 56:18-57:18 (emphasis added), attached as Ex. C.

[redacted]

Similarly, Dr. Bottorff did not know if the bioequivalence testing conducted by Aurobindo was on clean or contaminated valsartan:

[redacted]

Finally, Dr. Bottorff admitted had he didn't know if Torrent's valsartan was contaminated with nitrosamines when their bioequivalence studies were performed:

[redacted]

[9] Bottorff Dep. 3-25-2022, p. 84:11-85:4, attached as Ex. C.
[10] Bottorff Dep. 3-25-2022, p. 66:5-67:7; 68:19-69:2 (emphasis added), attached as Ex. C.

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[redacted]

[11] Bottorff Dep 3-25-2022, p. 57:20-58:5; 73:3-16; 82:9-83:8 (emphasis added), attached as Ex. C.

To add to the unreliability of Dr. Bottorff's conjecture that NDMA/NDEA contaminated VCDs are completely bioequivalent to noncontaminated versions, he conceded that his "impression" that the generic bioequivalence studies were conducted with valsartan containing nitrosamines was only based on vague discussions he had with counsel, but he had no documents to establish this conjecture and had no idea of the timeframe of how far back these drugs were contaminated. Dr. Bottorff testified as follows on the subject:

*****

[redacted]

Dr. Bottorff went on to testify that it doesn't matter if NDMA was in the valsartan tested, but if he had studies on contaminated valsartan that he would review them but wouldn't give them more weight than the studies on non-contaminated valsartan, and that bioequivalence studies on contaminated valsartan wouldn't change his conclusion. The following testimony further illustrates Dr. Bottorff's *ipse dixit* opinion:

[redacted]

[12] It didn't matter to Dr. Bottorff if the studies he was relying on were testing valsartan with nitrosamines, because he had already formed his opinion that nitrosamines wouldn't impact the bioequivalence of valsartan prior to looking at the studies. This is an *ipse dixit* opinion.
[13] Bottorff Dep. 3-25-2022, p. 90:24-94:13 (emphasis added), attached as Ex. C.

[redacted]

Furthermore, Dr. Bottorff did not review all of the bioequivalence studies (because he was not provided all of the documents that he requested to render his opinion), including studies in which generic valsartan that was contaminated with nitrosamines failed bioequivalence against name brand Diovan. Dr. Bottorff testified as follows when confronted with failed generic valsartan bioequivalence studies that he had not seen:

[redacted]

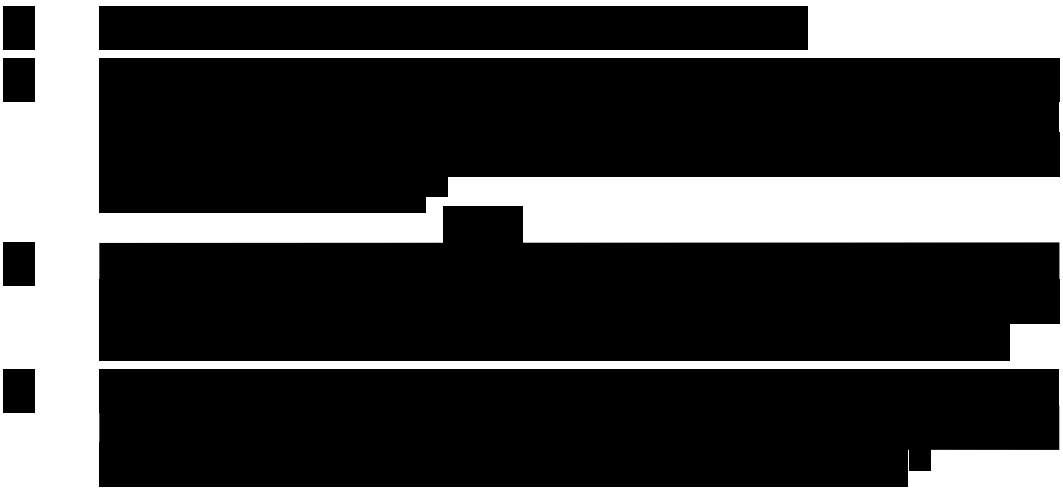
[14] Bottorff Dep. 3-25-2022, p. 79:8-80:20 (emphasis added), attached as Ex. C.

[redacted]

[15] Bottorff Dep. 3-25-2022, p. 161:23-164:10 (emphasis added), attached as Ex. C.

[redacted]

[16] Bottorff Dep. 3-25-2022, p. 191:15-197:9 (emphasis added), attached as Ex. C.



Dr. Bottorff has only unsupported conjecture and belief that these generic bioequivalence studies are support for the bioequivalence of NDMA/NDEA contaminated VCDs. He is unable to establish those studies were performed with contaminated valsartan drug product and *there are no research studies cited by Dr. Bottorff* that address whether nitrosamine contamination of VCDs changes the bioequivalence of valsartan drugs. The bioequivalence studies conducted on contaminated valsartan, which contradict Dr. Bottorff's opinion, were not provided to or reviewed by Dr. Bottorff. Without studies testing nitrosamine contaminated VCDs for their bioequivalence to the name brand drug (which did not contain nitrosamine contamination), there is no scientific support for Dr. Bottorff's opinion the contaminated version is bioequivalent, only Dr. Bottorff's unsupported belief. Unsupported beliefs do not satisfy the reliability standard of *Daubert* or constitute a reliable methodology. There are no "good grounds" for this opinion.

For these reasons, Dr. Bottorff's opinion that NDMA/NDEA contaminated VCDs have the same bioequivalence as the brand name drug cannot stand and must be precluded.

[17] Bottorff Dep. 3-25-2022, p. 197:25-199:14 (emphasis added), attached as Ex. C.
[18] Bottorff Dep. 3-25-2022, p. 225:15-24 (emphasis added), attached as Ex. C.

B. Dr. Bottorff's Expert Reports Do Not Render Any Opinion that Nitrosamine Contaminated VCDs Have the Same Monetary Value as the Uncontaminated Version

Dr. Bottorff's opinions are set forth in his January 12, 2022 expert report[19] and give no opinions about the monetary value or equivalence of contaminated VCDs. His expert report dated August 2, 2021,[20] sets forth his opinions and there are no opinions about the monetary value or equivalence of contaminated VCDs either. The failure to set forth an opinion on the monetary value of contaminated VCDs in either expert report renders such proffered opinion in violation of Rule 26(a)(2)(B) and is to be precluded.

This issue arose during Dr. Bottorff's deposition on September 16, 2021, when counsel sought to confirm no opinions were being rendered by him with respect to the monetary value of contaminated valsartan. At this deposition, Dr. Bottorff did offer an opinion that generic valsartan contaminated with NDMA or NDEA had the same monetary value as generic valsartan without these contaminants.[21] Defense counsel confirmed that Dr. Bottorff was not designated to be an expert witness on the issues of monetary value.[22] Dr. Bottorff also confirmed that he didn't express an opinion on monetary value and also confirmed he has no plan to testify to a jury that the monetary value of valsartan contaminated with nitrosamines is unchanged.[23]

Accordingly, it is requested that the Court confirm in its ruling that Dr. Bottorff will not be offering any opinions relative to the monetary value of contaminated VCDs in this action.

[19] Bottorff Report 1-12-2022. p. 52-53 attached as Ex. B.
[20] Bottorff Report 8-2-21, pp. 62-63, attached as Ex. A.
[21] Bottorff Dep. 9-16-2021, p. 14:3-24, attached as Ex. D.
[22] Bottorff Dep. 9-16-2021, p. 16:5-12, attached as Ex. D.
[23] Bottorff Dep. 9-16-2021, p. 16:18-24; p. 17:6-11, attached as Ex. D.

CONCLUSION

For the foregoing reasons, the above opinions of Dr. Michael Bottorff should be precluded by this Court.

Respectfully submitted,

By: /s/ C. Brett Vaughn

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CERTIFICATE OF SERVICE

I hereby certify that on March 13, 2023, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notifications of such filing to the CM/ECF participants registered to receive service in this MDL.

/s/ C. Brett Vaughn

C. Brett Vaughn, RN, BSN, JD